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$135M up front in latest pacts

‘Go-to for subcu’ Enhanze draws BMS, Roche money; Halozyme could reap $2B+

By Randy Osborne, Staff Writer

Halozyme Corp. CEO Helen Torley told *BioWorld* that she expects the latest news about the firm’s subcutaneous (subcu) hyaluronidase technology “on the heels of the Rituxan Hycela approval in June of this year by the FDA [will] spark even more rapid growth of companies wanting to sign an Enhanze deal.”

Six partners in hand already, San Diego-based Halozyme broke ground with a new arrangement

See Halozyme, page 3

Amgen drug gets FDA nod as first biosimilar to treat cancer

By Mari Serebrov, Regulatory Editor

The FDA triggered another biosimilar first Thursday with its right-on-schedule approval of Amgen Inc.’s Mvasi.

Not only is Mvasi the first biosimilar referencing Roche Holding AG’s blockbuster biologic Avastin (bevacizumab), it’s also the first biosimilar approved in the U.S. for the treatment of cancer.

The approval was not surprising, given the FDA’s positive comments to the Oncologic Drugs Advisory Committee in July and that committee’s unanimous vote of approval for the biosimilar that Amgen, of Thousand Oaks, Calif., developed in partnership with Dublin-based Allergan plc. (See *BioWorld*, July 14, 2017.)

Five of the six indications included in the approval were extrapolated. Mvasi was tested in nonsquamous, non-small-cell lung cancer (NSCLC), but it also was approved for first- or second-line treatment in metastatic colorectal cancer, second-line treatment for

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Astellas, Pfizer score a win on quest to extend Xtandi’s reach

By Michael Fitzhugh, Staff Writer

Swept ahead of schedule by a summer protocol amendment, a positive phase III trial of Xtandi (enzalutamide) in men with early stage castration-resistant prostate cancer (CRPC) is now providing key evidence that could back their inclusion in the drug’s label. Long desired by Astellas Pharma Inc. and Pfizer Inc., the partners behind Xtandi, the change could make about 20,000 more men eligible for on-label use of the drug in the U.S. each year alone, bolstering sales and further validating Pfizer’s $14.3 billion acquisition of Medivation Inc.

The trial, called Prosper, compared treatment of

See Xtandi, page 5

FDA’s latest accelerated nod clears Aliqopa, Bayer’s lymphoma drug

By Jennifer Boggs, Managing Editor

Bayer AG’s P13K inhibitor, copanlisib, won FDA approval Thursday for use in adults with relapsed follicular lymphoma who have received at least two prior systemic therapies.

It also marks the 11th cancer approval this year to come by way of the agency’s accelerated pathway.

Branded Aliqopa, copanlisib also was granted priority review and orphan designation by the FDA. It’s designed to target patients with the relapsed form of follicular lymphoma, a slow-growing type of non-Hodgkin lymphoma (NHL),

See Bayer, page 6

FDA workload demands lead to adjustments in Rx and biosimilar fees

By Mari Serebrov, Regulatory Editor

Reflecting a record-high workload at the FDA’s drug center, the reconstructed PDUFA fees for fiscal 2018 will have to generate more than $911 million in revenue over the next year.

PDUFA VI, as negotiated between the FDA and the prescription drug industry, called for $878.59 million as the base revenue amount to be raised by user fees in fiscal 2018, which begins Oct. 1. But by the time the base was adjusted to cover inflation, workload at the Center for Drug Evaluation and Research and commitment

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Newco News

‘Bare’-ish on naked effort, Nanology unveils particle approach across cancers

By Randy Osborne, Staff Writer

Nanology LLC’s strategy is “almost like having a new molecular entity, in terms of the broadness of the intellectual property [IP] around it, but on a more streamlined path to potential approval” if safety and efficacy pan out, Marc Iacobucci, managing director of DFB Pharmaceuticals Inc. told *BioWorld*, with a nod to the 505(b)(2) regulatory pathway that the Fort Worth, Texas-based firm intends to trod.

See Nanology, page 8

Financings

Array Biopharma Inc., of Boulder, Colo., said it commenced an underwritten public offering of $175 million of shares of its common stock. The company intends to grant the underwriters a 30-day option to purchase up to an additional $26.25 million of shares. J.P. Morgan Securities LLC and Cowen and Co. are acting as joint book-running managers with Piper Jaffray & Co. also acting as a bookrunner. Shares of Array (NASDAQ:ARRY) closed Thursday at $10.80, up 27 cents.

Biondvax Pharmaceuticals Ltd., of Ness Ziona, Israel, said it has priced an underwritten public offering of 1.5 million American depositary shares (ADSs), with each ADS representing 40 of its ordinary shares, at $6 per ADS. The company has granted the underwriter a 45-day option to purchase up to 166,667 additional ADS.

Curis Inc., of Lexington, Mass., said it priced an underwritten public offering of 20 million shares of its common stock and has granted the underwriter a 30-day option to purchase up to an additional 3 million shares of common stock. The share price was not disclosed. The company intends to use the net proceeds, together with its existing cash and investments, to continue development of CUDC-907, as well as CA-170, CA-327 and CA-4948 in collaboration with **Aurigene Discovery Technologies Ltd**., of Bangalore, India, and any additional product candidates for which it exercises its option to exclusively in-license from Aurigene, to fund potential acquisitions of new business, technologies or products that it believes will complement or expand its business, and for general working capital and capital expenditures. Shares of Curis (NASDAQ:CRIS) closed Thursday at $1.84, down 16 cents.

Epizyme, Inc., of Cambridge, Mass., said it priced an underwritten public offering of 9.18 million shares of its common stock at $15.25 each. In addition, the company has granted the underwriters a 30-day option to purchase up to an additional 1.37 million shares of common stock at the public offering price. Epizyme anticipates the total gross proceeds will be approximately $140 million, excluding any exercise of the underwriters' option. It anticipates using the net proceeds, together with its existing cash, cash equivalents and marketable securities, to fund global development costs of tazemetostat outside of Japan, including the costs of its ongoing and planned clinical trials and regulatory activities related to tazemetostat; to initiate supply chain and market development activities and prepare for the commercial launch of tazemetostat, if approved; to fund research and development costs to identify and develop other product candidates; and for working capital and other general corporate purposes. Shares of Epizyme (NASDAQ:EPZM) closed Thursday at $16, up 5 cents.

Grid Therapeutics LLC, of Durham, N.C., said it closed its series A financing and will use the proceeds to fund antibody production and a phase 1 trial of its lead candidate for the treatment of solid tumors. The financing was led by Longview International Ltd., a Singapore-based venture capital firm. Grid has developed an approach of identifying specific tumor immunoglobulin G antibodies from patients with early stage cancer. GT-103, the company's lead asset, is expected to enter a first-in-man phase I trial in advanced-stage solid tumor patients in early 2019.

Polarityte Inc., of Salt Lake City, said it is selling $15.2 million of series F convertible preferred stock at a conversion price of $27.50 per share; each investor will receive one half of a warrant exercisable at $30 per share. Skinte is the company's lead product in development for skin regeneration. Its investigational platform Polarityte, is being developed to simplify regeneration and allow tissue and cellular elements to function naturally. (See *BioWorld*, June 9, 2017.)

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Halozyme

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involving Bristol-Myers Squibb Co. (BMS), of New York: a global collaboration and license agreement to develop BMS immuno-oncology (I-O) medicines using Halozyme's Enhanze drug delivery approach, based on the recombinant human hyaluronidase enzyme, or rHuPH20. Using the compound can let drugs ordinarily given by the intravenous route be used subcu and, for those already given subcu, reduce the need for multiple injections.

Under the terms of the BMS arrangement, Halozyme will collect $105 million for access to Enhanze. BMS has designated multiple I-O targets, including PD-1, and owns an option to select up to 11 more targets within five years. Halozyme stands to earn milestone payments of up to $160 million for each target, and more for combo products, subject to achievement of specified development, regulatory and sales-based goals. If drugs are commercialized, BMS will pay royalties, too.

"They have selected some other targets, not named as yet," Torley said. "That's not uncommon in our deals," with partners holding back information for competitive reasons.

> *"Patients are living longer and better lives with great new therapies. What's holding them back is often the need to go back to an infusion center and spend half a day there.*
>
> Helen Torley
> CEO, Halozyme

Also, Halozyme is expanding a 2006 pact with Roche Holding AG, of Basel, Switzerland, which has agreed to license Enhanze for exclusive development of an undisclosed therapeutic target. Halozyme gets $30 million right away, with the chance to bank up to $160 million more if specified bells ring in the development, regulatory and sales areas. Included are tiered, mid-single-digit royalties.

Halozyme's first tie-up with Roche led to the pharma giant developing a pair of subcu formulations of cancer drugs for markets worldwide. More recently folded into the contract was the study of Halozyme's oncology drug, PEGPH-20 (a pegylated version of the same approach deployed by Enhanze), with Roche's Tecentriq (atezolizumab); a clinical collaboration started last year. Tecentriq is indicated for advanced urothelial carcinoma and in patients with metastatic non-small-cell lung cancer (NSCLC).

"Roche has selected all of the targets in that original agreement," Torley said, adding that the Swiss firm was "the company that helped us get where we are today with the success they've had with Rituxan [rituximab] and Herceptin [trastuzumab]."

The PEGPH-20 clinical collaboration will include the study of eight cancers in combo with Tecentriq, she said.

In June, the FDA cleared Roche's Rituxan Hycela (rituximab and hyaluronidase human) as a subcu injection for the treatment of adults with previously untreated and relapsed or refractory follicular lymphoma, previously untreated diffuse large B-cell lymphoma, and previously untreated as well as previously treated chronic lymphocytic leukemia. The new therapy includes the same monoclonal antibody as intravenous Rituxan in combination with hyaluronidase, thereby reducing administration time from 1.5 hours or longer to five to seven minutes.

Hycela involves a 10 mL to 15 mL injection, "but we also are used in a technology for Shire that's called Hyqvia, where patients can receive up to 300 mL in a subcu injection over an hour to get their entire month's dose of immune globulin," Torley said.

Halozyme's success has to do with "an increased recognition of two dynamics going on," she said. "Patients are living longer and better lives with great new therapies. What's holding them back is often the need to go back to an infusion center and spend half a day there. Sometimes the infusion centers are busy, and they actually get home without being treated. We're hearing there are examples of that."

Revenue projections doubled

Once a deal is signed, Halozyme serves mainly as an advisor to the company, "from the point of view of regulatory strategy and technical aspects of how to co-formulate the molecules," Torley said. Her firm makes the active pharmaceutical ingredient (API) and the rest is done by the partner, "with us meeting with them on a regular basis to offer advice. It isn't of high-resource intensity for us, except for the manufacture of the API."

Halozyme was "founded on the basis of attacking hyaluronan," substrate of hyaluronidase, Torley said. The two-sugar polymer is found throughout the body but "particularly under the skin," where it forms "a gel-like barrier" that prevents injecting large amounts of liquid. Enhanze technology temporarily degrades hyaluronan – a culprit that also accumulates around certain cancer cells and can impede the action of chemotherapy.

Enter PEGPH-20. In January, Halozyme reported top-line results from the combined analysis of stages 1 and 2 and stage 2 alone of its HALO-202 study as of December of last year. HALO-202 is a phase II, randomized, multicenter trial of lead investigational drug PEGPH-20 in combination with Abraxane (nab-paclitaxel, Celgene Corp.) and gemcitabine in stage IV pancreas cancer patients. Among the findings, the primary endpoints were achieved, showing a statistically significant increase in progression-free survival (PFS) for the efficacy evaluable population and by demonstrating a reduction in the rate of thromboembolic events in stage 2 of the study in the PEGPH-20 arm. The results were discussed at the American Society of Clinical Oncology meeting in Chicago this year, and a phase III trial is underway with PFS and overall survival as the two primary endpoints.

Phase Ib studies are ongoing with PEGPH-20 in NSCLC and gastric cancer in combination with Keytruda (pembrolizumab,

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Biosimilar

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metastatic colorectal cancer in patients who have progressed on a first-line bevacizumab-containing regimen, glioblastoma, metastatic renal cell carcinoma and cervical cancer.

Despite the extrapolations, Mvasi's label is not as expansive as that of Avastin, which also has been approved to treat platinum-resistant ovarian cancer and metastatic renal cell carcinoma. When the U.S. exclusivities on those indications end, Amgen would have to submit a data package to the FDA to support adding the indications to the Mvasi label.

As with Avastin, the Mvasi labeling contains a boxed warning about an increased risk of gastrointestinal perforations, surgery and wound healing complications, and severe or fatal pulmonary, gastrointestinal, central nervous system and vaginal bleeding.

Mvasi is the second Amgen biosimilar to get FDA approval. Its Amjevita, a biosimilar referencing Abbvie Inc.'s Humira (adalimumab), was approved a year ago. However, Mvasi is the first approval stemming from Amgen's collaboration with Allergan. The biosimilar also is under review in the EU. (See *BioWorld Today*, Sept. 27, 2016.)

Like Amjevita, Mvasi may have to wait on the market sidelines as patents are litigated or expire. "We are not providing launch details or pricing information at this time," an Amgen spokeswoman told *BioWorld*.

First approved in the U.S. in 2004, Avastin is protected by a thicket of patents with varying expiration dates, some of which stretch out more than a decade. A recombinant immunoglobulin G1 monoclonal antibody, Avastin binds to vascular endothelial growth factor (VEGF) and inhibits the interaction of VEGF with its receptors to inhibit the establishment of new blood vessels necessary for the survival and growth of solid tumors. The Roche blockbuster had sales of $6.85 billion last year, according to Cortellis.

Avastin may not be the only drug threatened by Mvasi's approval. A compounded version of Avastin is often used off-label as a cheaper alternative to Roche's more costly Lucentis (ranibizumab) in treating wet age-related macular degeneration. If Mvasi is used off-label in that manner, it could impact Lucentis, as well as Regeneron Pharmaceuticals Inc.'s Eylea (aflibercept). (See *BioWorld Today*, May 2, 2011, and Nov. 22, 2011.)

Meanwhile, Amgen and Allergan are collaborating on three more oncology biosimilars, and Amgen has another five biosimilars in its portfolio. ♦

Financings

Sophiris Bio Inc., of San Diego, said it entered a loan and security agreement with Silicon Valley Bank and may borrow up to $10 million in two term loans, with $7 million of that amount having already been accessed. At its discretion, the remaining $3 million can be borrowed subject to the achievement of certain milestones prior to Dec. 31, 2018. The term loans mature on Sept. 1, 2021. In connection with the loan, Sophiris issued to Silicon Valley Bank a warrant to purchase an aggregate of up to 99,526 of the company's common shares at an exercise price of $2.11 per share.

Summit Therapeutics plc, of Oxford, U.K., said it is conducting an underwritten public offering of 1.45 million American depositary shares (ADSs) at $12 per ADS. Each ADS represents five ordinary shares of Summit. The company has granted the underwriters an option for a period of 30 days to purchase up to an additional 218,850 ADSs. Gross proceeds from the offering are expected to be approximately $17.5 million – or $20.1 million if the underwriters exercise in full their option to purchase additional ADSs.

Other news to note

Ablexis LLC, of Burlingame, Calif., disclosed a license agreement with **Five Prime Therapeutics Inc.**, of San Francisco, granting the latter rights to use the Alivamab Mouse, a next-generation transgenic mouse platform for human therapeutic antibody discovery. Terms were not disclosed.

Astrazeneca plc, of London, said the FDA approved Symbicort (budesonide/formoterol fumarate dihydrate) inhalation aerosol 160 mcg/4.5 mcg to reduce exacerbations of chronic obstructive pulmonary disease (COPD). The drug is not indicated for the relief of acute bronchospasm. The new FDA approval is based on two phase IIIb studies of six-month and 12-month (Trial 4) duration, comparing the efficacy of Symbicort pressurized metered dose inhaler 160 mcg /4.5 mcg and formoterol 4.5 mcg, each administered as two inhalations twice daily in reducing COPD exacerbations in adult patients with moderate to very severe disease. First approved in 2006, Symbicort is indicated for asthma maintenance and COPD maintenance. In separate news, Astrazeneca, entered an agreement with **Aspen Global Inc.** (AGI), of Mauritius, part of the Aspen Group, under which AGI will now acquire the residual rights to the established anesthetic medicines comprising Diprivan, EMLA, Xylocaine/Xylocard/Xyloproct, Marcaine, Naropin, Carbocaine and Citanest. In June 2016, Astrazeneca entered an agreement with AGI under which AGI gained the exclusive commercialization rights to the medicines in markets outside the U.S. Under the terms of the new agreement, AGI will acquire the remaining rights to the intellectual property and manufacturing know-how related to the anesthetic medicines for an up-front consideration of $555 million. AGI will pay Astrazeneca up to $211 million in performance-related milestones based on sales and gross margin during the period from Sept. 1, 2017, to Nov. 30, 2019. Astrazeneca will continue to manufacture and supply the medicines to AGI during a transition period of up to five years, the company said.

Cannabis Science Inc., of Irvine, Calif., disclosed the publication of initial research results on using nanoparticle drones to target lung cancer with radiosensitizers and cannabinoids in *Frontiers in Oncology*. The publication addresses drug delivery, and highlights a strategy to transport cannabinoids directly to cancer cells with minimal toxicities or side effects that have so far hampered clinical translation efforts, the company said.

Xtandi

Continued from page 1

non-metastatic CRPC with the standard daily dose of 160 mg of Xtandi plus androgen deprivation therapy (ADT) to ADT alone. Top-line results showed that adding Xtandi to the mix improved metastasis-free survival, the trial's primary endpoint, by a statistically significant but so far undisclosed amount. Overall survival, a secondary endpoint in the study, will be analyzed and reported in the future.

Prosper enrolled about 1,400 men with prostate cancer that had progressed – based on a rising prostate-specific antigen level despite ADT – but who had no symptoms or evidence of metastatic disease. Though patients in the group targeted by the trial will often see a benefit for some period of time after ADT, their disease often will progress, Astellas spokesman Tyler Marciniak told *BioWorld*. "The jump to metastatic disease is a change," he said. Because of that, the partners thought that "if we could design a trial and show a benefit in delaying the radiographic appearance of these metastases, we believed there would be a benefit to patients for that," he said.

Evercore ISI analyst Umer Raffat told clients on Thursday that the trial is important because "it increases the target market size by perhaps more than double."

Xtandi is already approved for all forms of CRPC in Japan. But evidence generated by Prosper could help Astellas and Pfizer secure supplemental approvals that could help it reach about 20,000 or more patients in the U.S. and about 17,000 additional patients in European markets. Marciniak noted that publicly available patient segmentation data for the prostate cancer market is notoriously difficult.

Though originally slated to report in 2019, he said that "sample size and timelines were recently revised to reflect better odds of success based on evolving evidence from other trials – and the strategy clearly worked." The main purpose of the amendment was to revise the plan for the analyses of the primary and several secondary endpoints, allowing for a reduction in the target sample size in the trial to 1,440, from 1,560 patients.

Xtandi is an androgen receptor inhibitor for which Medivation first gained FDA approval in August 2012, with a label covering metastatic CRPC (mCRPC) in men who have previously received docetaxel. About two years later, in September 2014, FDA approval was granted for treatment of chemotherapy-naive mCRPC. Now, based on the results of Prosper, the companies intend to discuss the data with global health authorities to potentially support expanding the label for Xtandi to cover all patients with CRPC. So far, about 185,000 patients have been prescribed Xtandi.

As the partners continue their quest to expand Xtandi's reach into even earlier settings, they're also testing it in ongoing studies, such as the Arches trial in metastatic hormone-sensitive prostate cancer and the Embark trial in non-metastatic hormone-sensitive prostate cancer.

Last year, the drug generated $2.3 billion in sales globally. This year, sales appear to be maintaining momentum. According to Pfizer, the number of urologists actively prescribing Xtandi in a given month reached an all-time high in May. Astellas predicts that it will become the company's single largest revenue earner this year. Sales of the drug could hit nearly $3.2 billion globally by 2022, according to a consensus forecast compiled by Cortellis. (See *BioWorld Today*, April 26, 2017.)

> *"If we could design a trial and show a benefit in delaying the radiographic appearance of these metastases, we believed there would be a benefit to patients for that.*
>
> Tyler Marciniak
> Astellas spokesman

Astellas and Pfizer share equally in the gross profits related to U.S. net sales of Xtandi. For the most part, they also share equally in all Xtandi commercialization costs attributable to the U.S. market and certain development and other collaboration expenses. Pfizer receives tiered royalties as a percentage of international Xtandi net sales.

Should Prosper serve to help Astellas and Pfizer gain approval for Xtandi in early stage CRPC, still further expansions of the drug's label could lie ahead. Though breast cancers turned out to be a dead end for the drug early on, a phase II trial in hepatocellular carcinoma is ongoing, with a readout expected next year.

At least two additional phase III trials for non-metastatic CRPC are underway, including Janssen Research & Development's apalutamide (ARN-509). The trial, which started in March, is expected to read out in January 2023. Janssen picked up the second-generation androgen receptor degrader with its acquisition of Aragon Pharmaceuticals Inc. in the summer of 2013.

Additionally, Orion Corp. and Bayer AG are testing darolutamide (ODM-201/BAY-1841788) in a trial called Aramis. ♦

Other news to note

Daiichi Sankyo Co. Ltd., of Tokyo, and the University of Texas MD Anderson Cancer Center in Houston disclosed a multiyear collaboration focused on accelerating the development of therapies for acute myeloid leukemia (AML). The collaboration will focus on numerous clinical trials using several investigational compounds from the Daiichi pipeline and multiple agents in combination regimens. Compounds to be studied include quizartinib, a FLT3 inhibitor in late-stage clinical development, and three agents in early stage development: DS-3032, an MDM2 inhibitor; DS-3201, a dual EZH1/2 inhibitor; and PLX-51107, a BET inhibitor. Terms were not disclosed.

Bayer

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who are in need of further treatment options.

Intravenous Aliqopa is designed as a pan PI3K inhibitor, with predominant inhibitor activity against both PI3K-delta and PI3K-alpha isoforms.

The approval was based on data from a 104-patient, single-arm study in follicular B-cell NHL patients who had relapsed following at least two prior treatments. Data showed that 59 percent had a complete or partial response for a median of 12.2 months.

As part of the accelerated approval, Leverkusen, Germany-based Bayer will be required to confirm Aliqopa's benefit in further clinical studies. Those trials are ongoing.

The drug's cost has not been disclosed. Forecasts compiled by Cortellis Competitive Intelligence estimates worldwide 2018 sales of Aliqopa coming in at about $79.7 million, with annual sales growing to about $280 million by 2021.

Bayer has a number of other trials in the works, including midstage studies in NHL, diffuse large B-cell lymphoma, cholangiocarcinoma and endometrioid carcinoma, according to Cortellis.

Aliqopa's approval is just the latest in a spate of accelerated nods from the FDA. For 2017, BioWorld Snapshots has recorded 10 prior accelerated approvals in cancer, including three approvals for Keytruda (pembrolizumab, Merck & Co. Inc.) and two for Opdivo (nivolumab, Bristol-Myers Squibb Co.). Both those drugs target PD-1.

New molecular entities granted accelerated approval so far this year include Alunbrig (brigatinib, Takeda Pharmaceuticals Co. Ltd.), indicated for patients with metastatic ALK-positive non-small-cell lung cancer who have progressed or are intolerant to Pfizer Inc.'s Xalkori (crizotinib); EMD Serono Inc.'s Bavencio (avelumab), a PD-L1 inhibitor for treating adults and pediatric patients, 12 and older, with metastatic Merkel cell carcinoma; and Imfinzi (durvalumab), a PD-L1 inhibitor from Astrazeneca plc, approved to treat patients with locally advanced or metastatic urothelial carcinoma. (See *BioWorld Today*, March 24, 2017, and May 2, 2017.) ♦

Other news to note

Emerald Health Pharmaceuticals Inc., of San Diego, disclosed its plan to pursue synthetic cannabinoid-derivative drug candidates to treat life-threatening diseases. Formed in 2017, the privately held company has brought together a core team of experts in pharmaceutical drug development and cannabinoid research to develop its intellectual property to address a number of unmet medical needs, Emerald said. The firm has acquired two families of new chemical entities derived from cannabidiol (CBD) and cannabigerol (CBG), along with four related patents and patent applications. Two cannabinoid molecular backbones form the basis for the two families of compounds. Three recently granted patents and one pending patent associated with those molecules cover composition of matter relating to CBD and CBG derivatives, mechanisms of action, and their uses in multiple medical conditions associated with those mechanisms of action, Emerald said, adding that the families were acquired from **Vivacell Biotechnology España SL**, of Cordoba, Spain.

G3 Pharmaceuticals Inc., of Lexington, Mass., said it started an R&D program to pursue galectin-3 inhibitors. Galectin-3 is a protein that is responsible for fibrosis forming in the heart and kidney, which impairs organ function, leading to heart failure, atrial fibrillation and impaired kidney function.

Global Genomics Group LLC, of Richmond, Va., and Semmelweis University in Budapest, Hungary, said they have uncovered the degree of genetic heritability vs. environmental influences on the deposition of fat in different compartments of the human body. The findings were reported in the *International Journal of Obesity*, from the Budapest-Global study, co-led by the two entities. The study found that deposition of fat in different body compartments is under strong genetic influence, with epicardial (fat around the heart), subcutaneous (fat under the skin) and visceral adipose tissue (fat around the internal organs) being 80 percent, 78 percent and 70 percent determined by inherited genetic factors, Global Genomics said. The investigators also found that deposition of fat in the different body compartments is not independent of each other. The findings were derived from a classical twin study of 180 twin subjects from the study, and were based on analysis of the combined inheritance of complex traits.

Heat Biologics Inc., of Durham, N.C., was granted a 180-day extension by Nasdaq to meet the requirements for continued listing on its exchange. Heat received notice on March 15 that it was not in compliance with the minimum bid price requirements of $1 for 30 consecutive business days. At the time, Heat was afforded 180 calendar days, or until Sept. 11, to regain compliance.

Immunocellular Therapeutics Ltd., of Los Angeles, said the NYSE MKT accepted its plan to regain compliance with continued listing standards, granting the company until Dec. 23, 2018, to comply with its initiatives. Immunocellular's common stock will continue to trade on the NYSE MKT under the symbol IMUC, with the added designation of .BC to indicate that the company is not in compliance with listing standards.

Intarcia Therapeutics Inc., of Boston, and **Numab Therapeutics AG**, of Pfäffikon, Switzerland, said they achieved the first major milestone in their ongoing development partnership by selecting a multispecific antibody construct targeting autoimmune and inflammatory diseases. The event triggered a payment to Numab, bringing its payments for the project to CHF11.5 million (US$11.9 million).

Mars Innovation (MI), of Toronto, and **Evotec AG**, of Hamburg, Germany, launched LAB150 to shorten drug discovery timelines and to generate startup companies emerging from MI's 15 member institutions. MI will identify projects and build technical and business cases from scientific concepts focused on disease-related biological pathways. Evotec will contribute infrastructure and preclinical drug development expertise.

PDUFA

Continued from page 1

enhancements, the amount to be raised by the user fees increased nearly 4 percent.

The number of new drug applications (NDAs) and biologic license applications (BLAs) at the FDA this year is equal to the highest annual number recorded since the workload adjuster methodology was put into use in 2003, according to a *Federal Register* notice published Thursday.

On top of that, the number of active commercial investigational new drug applications (INDs), efficacy supplements and meetings/written responses only (WROs) hit a record high this year. And the manufacturing supplement count is only 2 percent below the highest number recorded since 2003.

Compared with just three years ago, NDAs/BLAs are up 12 percent, active commercial INDs are 10 percent higher, efficacy supplements are 25 percent higher, manufacturing supplements are 15 percent higher, and meetings scheduled/WROs are 27 percent higher.

Meanwhile, the FDA reduced how much it will need in fees for its biosimilar program, dropping the base amount of $45 million agreed to under BsUFA II to $40.2 million. The adjustment reflects an "updated assessment of the likely workload for the BsUFA program in FY 2018," the agency said in the *Federal Register* notice.

That's not to say interest in biosimilars is fading. Based on the $22.7 million it expects to raise in biosimilar application fees next year, the FDA is anticipating about 13 applications in 2018. It also expects to invoice for nine program fees, which are assessed against biosimilars that are approved as of the beginning of the fiscal year. With Thursday's approval of Amgen Inc.'s Mvasi as a biosimilar to Avastin (bevacizumab), the FDA has approved seven biosimilars to date. It indicated that two more may be approved before the end of this month. (See related story.)

In addition, the agency plans to raise nearly $14.77 million through the annual biosimilar biologic product development (BPD) fee that's assessed against each candidate that's filed an IND and is under development.

The agency said 55 candidates already are subject to the fee and 10 new biosimilars are expected to begin development in 2018.

The five-year FDA Reauthorization Act, which became law last month, substantially changed both the PDUFA and BsUFA fee schedules, so it's difficult to compare the fees with those charged in previous years.

Under the new structure, the 2018 PDUFA fees include $2,421,495 for applications requiring clinical data, $1,210,748 for applications not requiring clinical data and a $304,162 program fee for approved NDAs/BLAs.

The biosimilars fee schedule for 2018 includes $227,213 for the annual BPD fee for candidates in development, $1,746,745 for an application requiring clinical data, $873,373 for an application not requiring clinical data and a $304,162 program fee for approved biosimilars.

The fee schedules for generic drugs and medical devices were issued last month. ♦

Other news to note

Mustang Bio Inc., of New York, a Fortress Biotech company, expanded its pipeline through an exclusive global license agreement with Fred Hutchinson Cancer Research Center (Fred Hutch) for use of a CAR T therapy related to autologous T cells engineered to express a CD20-specific chimeric antigen receptor. As part of the transaction, Mustang inked an investigator-initiated trial agreement to provide partial funding for a phase I/II trial at Fred Hutch to evaluate the safety and efficacy of the CD20 technology in patients with relapsed or refractory B-cell non-Hodgkin lymphomas. The trial is expected to begin in the fourth quarter. (See *BioWorld Today*, Feb. 3, 2017.)

RDD Pharma Inc., of New York, said the Department of Defense office of the Congressionally Directed Medical Research Programs has funded the Spinal Cord Injury Research Program Translational Research Award – clinical trial application. The grant of $1.28 million will enable initial U.S. clinical development of RDD-0315 for fecal incontinence in spinal cord injury patients, including preparations for and conducting of a phase I study in healthy volunteers to assess acute tolerance and pharmacokinetics.

Reata Pharmaceuticals Inc., of Irving, Texas, said the FDA granted orphan designation to omaveloxolone to treat stage IIb through IV malignant melanoma. The company is running a phase Ib/II trial to evaluate the safety and efficacy of omaveloxolone in combination with Opdivo (nivolumab) or Yervoy (ipilimumab), both from **Bristol-Myers Squibb Co.**, of New York, in patients with unresectable or metastatic melanoma who failed anti-PD-(L)1 therapies.

Seqirus Inc., of Cambridge, Mass., said the FDA approved Afluria Quadrivalent (influenza vaccine) for use in people, age 5 and older. The product, indicated for protection against two influenza A strain viruses and two B strain viruses, first gained approval in August 2016 for people 18 and older.

Sunovion Pharmaceuticals Inc., of Marlborough, Mass., said the FDA approved the supplemental NDA to expand the indication for its antiepileptic drug, Aptiom (eslicarbazepine acetate), to include treatment of partial-onset seizures in children and adolescents, ages 4 to 17. The approval is based on FDA guidance that permits the extrapolation of data to support pediatric use.

Transcelerate Biopharma Inc., of Philadelphia, said **Novartis AG**, of Basel, Switzerland, joined the nonprofit consortium, which now includes 19 biopharmaceutical companies. At the same time, Elliott Levy, senior vice president of global development at **Amgen Inc**., of Thousand Oaks, Calif., was named chairman and David Nicholson, executive vice president and chief R&D officer at **Allergan plc**, of Dublin, assumed the role of vice chairman. (See *BioWorld Today*, Feb. 11, 2016.)

Nanology

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Taking aim at local delivery of chemotherapy via naked nanoparticles, Nanology was formed in collaboration with engineering firm Crititech Inc., of Lawrence, Kan., and product developer US Biotest Inc., of San Luis Obispo, Calif., with funding from DFB, also of Fort Worth. US Biotest is serving as Nanology's clinical/regulatory arm, Iacobucci said. "They're helping us manage the process of the six clinical trials that we have underway. DFB is doing the financing and the overall project management, and Crititech is doing the formulation development."

Specifically, Nanology has come up with sterile suspension forms of Nanopac (nanoparticle paclitaxel) and Nanodoce (nanoparticle docetaxel) as well as an inhaled form of Nanopac. A topical version of the latter, identified as SOR-007 ointment, was developed by affiliate DFB Soria LLC and licensed to Nanology. Six phase II trials are underway in a handful of indications. Nanology's patented nanoparticle production technology platform reduces the size of unprocessed paclitaxel and docetaxel crystals by up to 400 times into stable, naked nanoparticles, with an exponential increase in surface area and unique geometry.

The usual form of paclitaxel "is already in a dissolved state," Iacobucci said. "You inject it in and it's just going to leak out in the area, whereas what we're injecting are small particles that stay at the site and slowly dissolve over time. We have high hopes."

> *"Everything that we are doing right now is pretty much fully funded.*
>
> Marc Iacobucci
> Managing Partner, DFB Pharmaceuticals

Many direct-injection bids, "at least what I'm aware of, they're taking a systemic agent – maybe a known agent or a new agent – but it's the retention in the tumor that becomes the issue," he said. "Normally it's not particles that are being injected but some type of dissolved substance where you're governed by the half-life, the normal half-life of that material. Our particles get entrapped in the tumor," seeping into it gradually. "We have studies, for example, with nanoparticles injected into the peritoneum, where drug remains [there,] dissolving over more than four weeks. The clearance, though, is at a level that's so low that it's always subtoxic. You can hardly measure it."

Even better, the company has "some evidence to support [the idea] that the clearance is partially through the lymphatic system, which could be very exciting in its own right," since cancer follows that system to metastasize, he said.

"Conventionally, when you make small particles, you're using a milling process or some other mechanical means that imparts a static charge and energy to the particles, and so coating agents are used in order to keep the particles themselves stable," Iacobucci said. "Coating agents are also used in most small particle applications for drugs to help impact bioavailability [as well]. What really intrigued us initially is the way Crititech was looking at what we now call a naked nanoparticle. Their technology allows the formation of very small particles, but no static charge or energy is imparted to the molecule during this process. The particles essentially precipitate out, and the powder is free-flowing, so it can be suspended just prior to use in a simple vehicle like saline."

Such chemo agents as paclitaxel and docetaxel have toxicity limitations when deployed systemically. It was Crititech that did the phase I trial in ovarian cancer where chemo in suspension was administered into the peritoneum.

"When we began the collaboration in 2015, we looked to broaden this into a platform, so we looked at different ways to use the nanoparticle," Iacobucci said. "Now we have begun clinical trials in prostate and pancreatic cancers, where we're going to be delivering the drug directly to the site of the tumor. For pancreatic cancer, we're going through endoscope and ultrasound-guided fine needle injection." A similar route will be used in prostate cancer. "Both of these procedures are well known," he said. "With the prostate, ultrasound-guided injection of radioactive seeds and things like that are well-described."

Works with other molecules, too

Progress has been made "with all of the abdominal imaging procedures over the last 10 years or so, [and] there has been more and more information garnered on pancreatic cysts," Iacobucci said. "They're common, and a certain percentage of cysts – it's a small percentage – can lead to pancreatic cancer. In today's day and age, that's a death sentence. There is no real approved procedure that exists for pancreatic cysts," and surgeons often try aspiration, injecting ethanol with a view to destroying the epithelial lining, he said. Nanology would inject its nanoparticle suspension instead.

Topical SOR-007 is in the works for actinic keratosis and cutaneous metastases. "We're focused mainly on breast cancer," Iacobucci said. "These are patients that have metastatic disease, and sometimes the metastases present themselves as lesions on the skin. In addition to having a serious disease, you've got the indignity of these skin eruptions. Paclitaxel is effective against many forms of breast cancer," so it makes sense that the drug might help with lesions.

Regarding the inhaled product, "we've shown that it's delivered effectively to the lungs" via nebulizer, he said. "It's retained in the lungs for a long period of time." A preclinical experiment is ongoing and Nanology intends to develop the compound in non-small-cell lung cancer, if all goes well. The company has "very favorable pharmacokinetic data that I can't get into right now, because we want to make sure that we've got intellectual property surrounding [it]," he said.

DFB was formed at the end of 1990 by Chairman and CEO Paul

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Halozyme

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Merck & Co. Inc.), as well as in breast cancer when paired with Halaven (eribulin, Eisai Inc.).

Torley said she wants Halozyme to become the "go-to" company for subcu formulations. The class of monoclonal antibodies is where Enhanze is "mostly being used to date, in all sorts of disease areas, even outside of oncology," but "we see many molecules out there in leading companies" that could benefit across drug types, and the firm is "in active discussions with a number" of them, she said.

"We're feeling very good about our current situation" financially, Torley said, noting that the most recent deals have doubled Halozyme's revenue projections for this year while leaving expense guidance unchanged. The firm is "moving into a positive cash flow situation," she said. "We estimate year-end having $380 million to $395 million in cash. That's a very healthy balance for the company to get our work done."

Shares of Halozyme (NASDAQ:HALO) closed Thursday at 15.98, up $2.80, or 21.2 percent. ♦

Coming Monday in *BioWorld Insight*

Therapies for mitochondrial disease are advancing in clinic

While advocacy activities to raise awareness about mitochondrial diseases around the world are ongoing, those efforts get a boost each year during the third week of September, which is dedicated to Mitochondrial Disease Awareness Week. Its aim is to increase the spotlight on the need for more research to uncover new therapies. Understanding mitochondrial disease, which is estimated to affect one in 4,000 people, remains a significant challenge because of the diversity of human disorders at every level – clinical and genetic – that result when the mitochondria of the cell cannot produce the energy the body needs to support growth. Progress, however, is being made with a growing number of companies active and advancing their lead products in clinical trials, and many more planning preclinical programs.

Bad combo for heart drugs: Approvals down, take longer

The approval success rate for cardiovascular drugs fell from about 5.2 percent for drugs entering the clinic during 1995-2000 to 2.2 percent for those that started trials during 2001-2007, while the length of time from entering the clinic to approval increased substantially, according to a new study from the Tufts Center for the Study of Drug Development. The culprit: a need to show an incremental benefit over the current low-cost generic treatments that work fairly well.

Nanology

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Dorman and a couple of partners, Iacobucci said. "It started as a contract development and manufacturing organization, and from that Paul and a group of management – I'm one of them, I've been with the company since the end of 1992 – created several different operating companies, and took the business from [being worth] about $18 million to $400 million or so by the mid-2000s, and then eventually divested the main operating companies by the end of 2012, realizing well over $1 billion value," he said.

"At that time, one of the partners retired and Paul, who was always the major part of DFB, decided to create a new vision," putting together "a pretty significant amount of seed money to take this work at least through phase II clinical trials. Everything that we are doing right now is pretty much fully funded," Iacobucci said. "We're going to be generating efficacy data along the way. We have just begun now to formally announce Nanology to the pharmaceutical industry." The firm will determine what's next as the data begin to roll out. Nanology has considered "investing ourselves to take this forward or trying to find a big pharma partner that has an interest in oncology. We haven't made any decisions on that, but we have options."

Crititech "demonstrated that this technology can work for a number of molecules," Iacobucci noted. "That said, it doesn't work for every kind of molecule, [but] the platform itself, what we're doing, [with] suitable agents could definitely accomplish the same thing. We have a number of molecules on the drawing board, but we are not intending to advance anything else until we get through this program. It's a lot on the plate."

Those involved with DFB from the start grew the company to about 1,500 people. "There are four of us left at DFB," Iacobucci said.

"We're participating with three of the principals at Crititech and a couple at US Biotech. That forms the core [Nanology] company. We're leveraging relationships that we have across the industry, almost on a virtual basis, to progress these trials," he said. ♦

In the clinic

Alexion Pharmaceuticals Inc., of New Haven, Conn., reported results from an interim analysis of the ongoing extension of the phase III REGAIN trial testing Soliris (eculizumab), a complement inhibitor, in patients with refractory generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor antibody-positive at the annual meeting of the American Association of Neuromuscular & Electrodiagnostic Medicine in Phoenix. Across all four assessment scales – MG-Activities of Daily Living, Quantitative MG, MG Composite and MG Quality of Life 15 – the benefits of Soliris seen in REGAIN were maintained after 52 weeks of treatment for the 20 patients that remained in the extension study. Twenty patients who received placebo in the REGAIN trial improved on all four assessment scales after switching to Soliris in the extension study, which was maintained at week 52.

In the clinic

Alk-Abelló A/S, of Copenhagen, Denmark, reported data from a phase III trial testing its tree allergy sublingual immunotherapy (SLIT) tablet in 634 patients with birch pollen allergic rhinitis and/or conjunctivitis. Treatment with the tree SLIT-tablet reduced the total daily combined score, defined as the sum of the allergic symptom score and the use of symptom-relieving medication, during the birch pollen season by 39.6 percent compared to placebo. The efficacy was similar during the entire tree pollen season, including the alder and hazel pollen seasons. Alk plans to submit a marketing application to European and possibly Canadian regulators in 2018.

Astrazeneca plc, of London, reported data at the European Association for the Study of Diabetes meeting in Lisbon, Portugal, from the EXSCEL (EXenatide Study of Cardiovascular Event Lowering) trial that showed cardiovascular safety with Bydureon (exenatide extended-release) in patients with type 2 diabetes at a wide range of cardiovascular (CV) risk. Exenatide once-weekly did not increase the incidence of major adverse cardiovascular events (MACE), a composite endpoint of CV death, nonfatal heart attack or nonfatal stroke, compared to placebo ($p<0.001$ for noninferiority). There were also fewer CV events observed in the exenatide arm of the trial (839 [11.4 percent] vs. 905 [12.2 percent]), although the primary efficacy objective of a superior reduction in MACE narrowly missed statistical significance ($p=0.061$).

Atossa Genetics Inc., of Seattle, reported preliminary results from its phase I, dose-escalation study showing that topical endoxifen met all objectives. There were no clinically significant safety signals and no clinically significant adverse events in participants receiving topical endoxifen, and the product was well-tolerated at each dose level and for the dosing duration. The topical drug, an active metabolite of tamoxifen, was able to cross the skin barrier when applied daily to the breast, as demonstrated by low but measurable endoxifen blood levels detected in a dose-dependent fashion. Atossa expects to announce results from the oral arm of the study in the next 30 to 60 days.

Biovie Inc., of Beverly, Mass., enrolled the first patient in its phase IIa trial testing BIV-201 (terlipressin) in six patients with refractory ascites due to liver cirrhosis. The trial, which is scheduled to complete early next year, will measure safety and pharmacokinetics of terlipressin's active metabolites as well as measuring the number of paracentesis procedures and the amount of ascites fluid generation.

Bone Therapeutics SA, of Gosselies, Belgium, reported interim data from a phase IIa trial testing its allogeneic cell therapy product, Allob, in 15 patients undergoing a lumbar spinal fusion. All 15 patients had an absence of motion at the treated level 12 months after treatment. Nine of the 15 patients had continuous bone bridges as measured with CT scans with the other six having evidence of bone formation without continuous bony bridging. The Oswestry Disability Index decreased by a mean of 55 percent compared to baseline with back and leg pain reduced by 59 percent and 90 percent, respectively. Bone Therapeutics plans to complete enrollment of the trial at 32 patients by the end of 2017 or early 2018. Given the strong phase IIa data, the company plans to halt recruitment for its exploratory study in rescue treatments for failed spinal fusion and close the study upon completion of the follow-up of existing patients.

Dermira Inc., of Menlo Park, Calif., and **UCB SA**, of Brussels, Belgium, reported data from three phase III trials testing Cimzia (certolizumab pegol), which targets tumor necrosis factor-alpha, in patients with moderate to severe chronic plaque psoriasis at the 26th European Academy of Dermatology and Venereology Congress in Geneva. Patients in the CIMPASI-1, CIMPASI-2 and CIMPACT trials who responded after 16 weeks of treatment with Cimzia maintained their clinical benefit, quality of life, and work productivity and activity impairment measures through 48 weeks of treatment. UCB also presented data from its CRIB and CRADLE studies showing that there was no placental transfer of Cimzia from mother to fetus during pregnancy and minimal to no transfer of the drug into breast milk. Cimzia is currently under review by the FDA and the EMA as a treatment for patients with moderate to severe chronic plaque psoriasis. (See *BioWorld Today*, Jan. 20, 2017.)

Eli Lilly and Co., of Indianapolis, and **Incyte Corp.**, of Wilmington, Del., reported phase II data testing baricitinib in patients with moderate to severe atopic dermatitis at the 26th European Academy of Dermatology and Venereology meeting in Geneva. Baricitinib plus a topical corticosteroid (TCS) produced a 50 percent or greater reduction in the overall disease severity as measured by the Eczema Area and Severity Index in 61 percent of the 38 patients treated with the combination compared to 37 percent of the 49 patients treated with TCS alone. Lilly plans to start a phase III program for moderate to severe atopic dermatitis later this year. In April, the companies received a complete response letter for baricitinib as a treatment for rheumatoid arthritis. (See *BioWorld Today*, April 17, 2017.)

Imara Inc., of Cambridge, Mass., reported preclinical and phase I data for its sickle cell disease (SCD) treatment, IMR-687, at the 6th Annual Sickle Cell Therapeutics Conference in New York. In mouse models, IMR-687, a phosphodiesterase 9 inhibitor, reduced red blood cell sickling and white blood cell adhesion and increased fetal hemoglobin. The drug also reduced blood vessel occlusion. A phase I trial in healthy volunteers showed IMR-687 was safe and well-tolerated at a dose that exceeded the effective doses in cell and animal models of SCD. Imara plans to start a phase II trial testing IMR-687 in adults with SCD by the end of the year.

Innovation Pharmaceuticals Inc., of Beverly, Mass., said it opened a new clinical site for its phase II trial testing Kevetrin in patients with ovarian cancer. The trial will measure treatment-emergent adverse events as well as changes in cancer pathway biomarkers and molecular signatures after treatment with Kevetrin, a p53 modulator. Preliminary results from the trial are expected in the fourth quarter of 2017.

In the clinic

Leo Pharma A/S, of Ballerup, Denmark, reported results from the AMAGINE-2 extension trial testing Kyntheum (brodalumab) in patients with moderate to severe plaque psoriasis at the 26th European Academy of Dermatology and Venereology Congress in Geneva. Treatment with Kyntheum, a monoclonal antibody targeting IL-17 receptor subunit A, for 120 weeks produced completely clear skin (PASI 100) in 56.2 percent and almost clear skin (PASI 90) in 76.8 percent of the 779 patients in the trial, compared to 53 percent and 78 percent of patients achieving PASI 100 and PASI 90 after one year of treatment, respectively. Leo also reported pooled analysis of the phase III AMAGINE-1, -2 and -3 trials showing that 59 percent of patients taking Kyntheum reported their psoriasis had no impact on their overall quality of life compared to 6 percent of patients on placebo.

Levicept Ltd., of Sandwich, U.K., started a phase I trial testing LEVI-04, a p75 neurotrophin receptor fusion protein, in healthy volunteers and osteoarthritis patients. The 56-patient dose-escalation trial will start in healthy volunteers at the lowest three doses, before being tested in patients with osteoarthritis at dose three and higher. Safety and tolerability will be assessed as the primary endpoints, with pharmacokinetics and pharmacodynamics also being measured. The trial is scheduled to be completed in early 2019.

Medivir AB, of Stockholm, said the independent data monitoring committee again recommended continuation of the MIV-711 osteoarthritis extension study without modifications based on a review of the accumulated safety data. That marks the sixth and final review planned for the trial. MIV-711 is being developed as a disease-modifying agent for osteoarthritis.

Oncbiomune Pharmaceuticals Inc., of Baton Rouge, La., said the phase Ia trial of Proscavax met its primary objective of no dose-limiting adverse events 30 days post-final vaccination in any of the 20 patients receiving six vaccinations per protocol. The study, which is testing Proscavax for safety and tolerability in recurrent prostate cancer patients with increasing prostate-specific antigen (PSA), also reported no serious adverse events. Secondary objectives suggest efficacy in treating late-stage prostate cancer. At a median follow-up of 31 months post-final vaccination, nine of the 14 evaluable patients (64.3 percent) who received all six vaccinations had increased PSA doubling time, suggesting Proscavax was slowing tumor growth. Twelve of 15 patients (80 percent) completing the protocol had an increased immune response to PSA as determined with a lymphocyte blastogenesis assay. Proscavax, an immunotherapeutic cancer vaccine, combines prostate cancer-associated PSA with the biological adjuvants interleukin-2 and granulocyte-macrophage colony-stimulating factor.

Oncolytics Biotech Inc., of Calgary, Alberta, said the first patient was treated in the phase Ib trial, MUK eleven, studying oncolytic virus candidate Reolysin (pelareorep) in combination with immunomodulatory drugs (IMiDs) Revlimid (lenalidomide, Celgene Corp.) and Imnovid (pomalidomide, Celgene Corp.) as a rescue treatment in relapsing myeloma patients. The trial will enroll about 44 patients and will study the combination in patients whose myeloma is progressing while being treated with one of those IMiDs. It will measure safety and tolerability as well as investigate whether the addition of Reolysin extends disease control in that patient group.

Phrixus Pharmaceuticals Inc., of Ann Arbor, Mich., said it inked deals with several Duchenne muscular dystrophy (DMD) patient organizations and Cincinnati Children's Hospital to conduct a first clinical trial of Carmeseal-MD (the active pharmaceutical ingredient is poloxamer 188 NF), for the treatment of DMD in non-ambulatory patients. A number of endpoints will be evaluated, including effects of the product on respiratory endpoints such as forced vital activity and on secondary endpoints related to cardiac and skeletal limb muscle performance.

Poxel SA, of Lyon, France, reported results at the European Association for the Study of Diabetes meeting in Lisbon, Portugal, from the imeglimin phase IIb study in Japan, showing consistent, statistically significant ($p<0.0001$) decreases at the top two doses in the key secondary endpoints of fasting plasma glucose, glycated albumin and percentage of patients reaching a target HbA1c of less than 7 percent. A statistically significant dose-dependent (500 mg $p=0.008$, 1,000 mg $p=0.0008$ and 1,500 mg $p<0.0001$) improvement of the homeostasis model assessment of beta cell function, a marker of beta cell function in fasting condition, was also observed. In addition, there was a significant decrease in two of the most relevant liver enzymes, alanine aminotransferase and gamma-glutamyl transferase, which are considered biomarkers in liver disease.

Sandoz, of Holzkirchen, Germany, a Novartis AG unit, reported data on its proposed biosimilar of Humira (adalimumab, Abbvie Inc.), with results from a long-term study of patients continuously treated with the biosimilar or the reference medicine showing that efficacy and safety profiles of the two medicines match throughout 51 weeks of treatment in patients with moderate to severe chronic plaque psoriasis. Results were presented at European Academy of Dermatology and Venereology meeting in Geneva.

Sanofi SA, of Paris, reported data at the European Association for the Study of Diabetes meeting in Lisbon, Portugal, from the randomized trial TAKE CONTROL, showing that type 2 diabetes patients had better control of blood sugar (HbA1c) without increasing the risk of hypoglycemia when using Toujeo (insulin glargine 300 units/mL, Gla-300) with a simple dose-titration regimen, compared with patients whose dose adjustment was managed by their physician. After six months, patients with type 2 diabetes who used patient-driven titration achieved improvement of HbA1c ($p=0.0247$) compared with those who followed physician-driven titration. The proportion of patients reaching the pre-defined blood glucose target without experiencing severe and/or confirmed hypoglycemia was 67.5 percent in the patient-driven titration group, compared with 58.4 percent in the group using physician-driven titration ($p=0.0187$). Similar proportions of patients in both groups (6.4 percent vs. 6.3 percent), experienced at least one severe and/or confirmed (<54 mg/dL) hypoglycemic event.

In the clinic

Sellas Life Sciences Group Ltd., of Hamilton, Bermuda, said its WT1-targeting immuno-oncology treatment, galinpepimut-S, led to mounting of specific, potent and durable immune responses (IRs) in multiple myeloma (MM) patients in phase II testing. Both the rate (frequency) and potency of the durable IRs in MM patients were correlated with clinical benefit accorded by galinpepimut-S, defined as achievement of clinical complete response or very good partial response in patients who completed per protocol immunizations (12 doses). Data were presented at the Society of Hematologic Oncology meeting in Houston, and published in *Clinical Lymphoma, Myeloma & Leukemia*. Galinpepimut-S is currently expected to enter a pivotal phase III trial in patients with acute myeloid leukemia and is in various development phases in MM and ovarian cancer.

Vanda Pharmaceuticals Inc., of Washington, reported results from an eight-week, randomized phase II study of tradipitant, an oral neurokinin-1 receptor antagonist, as a monotherapy in the treatment of chronic pruritus in patients with atopic dermatitis. Tradipitant was shown to improve the intensity of the worst itch patients experienced, as well as atopic dermatitis disease severity. Significant improvements were observed in the measurement of Worst Itch Visual Analog Scale (VAS) (p=0.019). Tradipitant also showed significant effects in a responder analysis for Worst Itch in patients who achieved improvements of greater than or equal to 40 points improvement from baseline in Worst Itch VAS scores (p=0.037) or greater than or equal to 30 points (p=0.049). On the pre-specified primary endpoint of Average Itch VAS, tradipitant showed improvement over placebo, but that improvement was not significant due to a high placebo effect and the lack of sensitivity of that measure. Vanda said it expects to meet with the FDA to further define a path toward registration.

Appointments and advancements

Achillion Pharmaceuticals Inc., of New Haven, Conn., named Joseph Truitt chief operating officer, and Avner Ingerman senior vice president and head of ophthalmology.

Albany Molecular Research Inc., of Albany, N.Y., appointed Stephen Leonard senior vice president, head of global operations.

American Gene Technologies International Inc., of Rockville, Md., added Julia R. Brown to its board.

Amphivena Therapeutics Inc., of South San Francisco, named Eric J. Feldman senior vice president, clinical development; Tae H. Han vice president, clinical pharmacology and translational medicine; and Deborah J. Tranowski vice president, program management and operations.

Chimerix Inc., of Durham, N.C., appointed Heather Knight-Trent vice president of regulatory affairs.

Minerva Neurosciences Inc., of Waltham, Mass., named Jay B. Saoud senior vice president, head of research and development.

Novelion Therapeutics Inc., of Vancouver, British Columbia, added Suzanne Bruhn to its board, effective Oct. 1.

Palatin Technologies Inc., of Cranbury, N.J., added Anthony M. Manning to its board.

PDL Biopharma Inc., of Incline Village, Nev., appointed Dominique P. Monnet president.

Tigenix NV, of Leuven, Belgium, appointed Gregory Gordon head of medical department (U.S.), and Annette Valles-Sukkar associate director, clinical project.